IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	H. Robert Horvitz et al.	Art Unit:	Not yet assigned
Serial No.:	09/888,243	Examiner:	Not yet assigned
Filed:	June 22, 2001	Customer No.:	21559

Title: RELATEDNESS OF HUMAN INTERLEUKIN-1β CONVERTASE GENE TO A *C. ELEGANS* CELL DEATH GENE, INHIBITORY PORTIONS OF THESE GENES AND USES THEREFOR

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DECLARATION OF KRISTINA BIEKER-BRADY, PH.D.

I, Kristina Bieker-Brady, Ph.D., state as attorney of record for the above-referenced patent application, and as a Registered Patent Attorney, the following:

1. The amino acid sequence of SEQ ID NO: 28 in the Amended Sequence Listing filed herewith is the amino acid sequence of murine NEDD-2 in Fig. 2 of Fernandes-Alnemri *et al., J. Biol. Chem.* 269:30761, 1994, a copy of which is enclosed with an enlarged version of Fig. 2. As indicated on page 32, lines 7-10, of the specification, this publication is incorporated by reference in the present application as a part of the definition of asp-ase proteases of the invention. As the amino acid sequence of SEQ ID NO: 28 is the same as that of the sequence incorporated by reference, this amendment contains no new matter.

2. In the preliminary amendment filed herewith, the numbering of the amino acid residues of the NEDD-2 proteins recited in claims 9-13 and 16 has been amended to correspond to the amino acid numbering of the NEDD-2 sequence of SEQ ID NO: 28. As illustrated in the sequence alignment of Exhibit A, residues 43, 44, 46, 67, 82, 97, 102, 103, 108, 122, 158, 163, and 166 of SEQ ID NO: 13 recited in claim 12 as filed (top sequence) correspond to residues 323, 324, 326, 327, 362, 377, 282, 383, 386, 388, 402, 438, 443, and 446, respectively, of SEQ ID NO: 28 recited in amended claim 12 (bottom sequence). Similarly, residue 117 of SEQ ID NO: 26 recited in claim 9 as filed corresponds to residue 397 of SEQ ID NO: 28 recited in amended claim 9.

The sequence alignment of Exhibit B indicates that the catalytic cysteine 303 of the NEDD-2 sequence deposited in Genbank as accession number P29594 (bottom sequence) corresponds to cysteine 319 of the NEDD-2 sequence of SEQ ID NO: 28, which has additional amino acids because of an earlier translation start site (top sequence). Thus, cysteine 319 of the NEDD-2 sequence of SEQ ID NO: 28, which is recited in amended claims 10, 11, 13, and 16, corresponds to the active site cysteine of NEDD-2.

Date: _January 16, 2002_

Kristina Bieker-Brady
Reg. No. 39,109

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Exhibit A

Seq1	Seq2	Similarity Index	Consensus Length
01997.11003. seq id 13 with ala	01997.11003.seq id 28	89.7	145
(27>171)	(307>451)		

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                    ▾30        ▾40        ▾50        ▾60        ▾70        ▾80        ▾90       ▾100       ▾110
LGTSFCSLLPPPLLLY  TDRGVDQQDGKNHTQSPGCEESDAGKEELMKMRLPTRSDMICGYACLKGNAAMRNTKRGSWYIEALTQVFSER
L             DRGVDQQDGKNHTQSPGCEESDAGKEELMKMRLPTRSDMICGYACLKGNAAMRNTKRGSWYIEALTQVFSER
LQNKPKMFFIQACRGDETDRGVDQQDGKNHTQSPGCEESDAGKEELMKMRLPTRSDMICGYACLKGNAAMRNTKRGSWYIEALTQVFSER
             ▴310       ▴320      ▴330      ▴340      ▴350      ▴360      ▴370      ▴380      ▴390
                                                        ▾120
                                                        ▾130
CDMHVADMLVKVNALIKEREGYAPGTEFHRCKEMSEYCSTLCQQLLFPGYPPT
CDMHVADMLVKVNALIKEREGYAPGTEFHRCKEMSEYCSTLCQQLLFPGYDPT
ACDMHVADMLVKVNALIKEREGYAPGTEFHRCKEMSEYCSTLCQQLLFPGYDPT
             ▴400      ▴410
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Ktuple: 2; Gap Penalty: 4; Gap Length Penalty: 12

Seq1(1>451)	Seq2(1>435)	Similarity	Gap	Gap	Consensus
01997.11003.seq id 28	01997.211003.nedd-2	Index	Number	Length	Length
(18>451)	(1>435)	99.5	1	1	435

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        ↙20        ↙30        ↙40        ↙50        ↙60        ↙70        ↙80
MAADRRSRILAVCGMHPDHQETLKKNRVVLAKQLLLSELLEHLLEKDIITLEMRELIQAKGGSFSQNVE-
MAADRRSRILAVCGMHPDHQETLKKNRVVLAKQLLLSELLEHLLEKDIITLEMRELIQAKGGSFSQNVE
MAADRRSRILAVCGMHPDHQETLKKNRVVLAKQLLLSELLEHLLEKDIITLEMRELIQAKGGSFSQNVEL
              ↖10        ↖20        ↖30        ↖40        ↖50        ↖60        ↖70

        ↙90       ↙100       ↙110       ↙120       ↙130       ↙140       ↙150
LNLLPKRGPQAFDAFCEALRETRQGHLEDLLLTTLSDIQHVLPPLSCDYDTSLPFSVCESCPPHKQLRLS
LNLLPKRGPQAFDAFCEALRETRQGHLEDLLLTTLSDIQHVLPPLSCDYDTSLPFSVCESCPPHKQLRLS
LNLLPKRGPQAFDAFCEALRETRQGHLEDLLLTTLSDIQHVLPPLSCDYDTSLPFSVCESCPPHKQLRLS
              ↖80        ↖90       ↖100       ↖110       ↖120       ↖130       ↖140

       ↙160       ↙170       ↙180       ↙190       ↙200       ↙210       ↙220
TDATEHSLDNGDGPPCLLVKPCTPEFYQAHYQLAYRLQSQPRGLALVLSNVHFTGEKDLEFRSGGDVDHT
TDATEHSLDNGDGPPCLLVKPCTPEFYQAHYQLAYRLQSQPRGLALVLSNVHFTGEKDLEFRSGGDVDHT
TDATEHSLDNGDGPPCLLVKPCTPEFYQAHYQLAYRLQSQPRGLALVLSNVHFTGEKDLEFRSGGDVDHT
              ↖150       ↖160       ↖170       ↖180       ↖190       ↖200       ↖210

       ↙230       ↙240       ↙250       ↙260       ↙270       ↙280       ↙290
TLVTLFKLLGYNVHVLHDQTAQEMQEKLQNFAQLPAHRVTDSCVVALLSHGVEGGIYGVDGKLLQLQEVF
TLVTLFKLLGYNVHVLHDQTAQEMQEKLQNFAQLPAHRVTDSCVVALLSHGVEGGIYGVDGKLLQLQEVF
TLVTLFKLLGYNVHVLHDQTAQEMQEKLQNFAQLPAHRVTDSCVVALLSHGVEGGIYGVDGKLLQLQEVF
              ↖220       ↖230       ↖240       ↖250       ↖260       ↖270       ↖280

       ↙300       ↙310       ↙320       ↙330       ↙340       ↙350       ↙360
RLFDNANCPSLQNKPKMFFIQACRGDETDRGVDQQDGKNHTQSPGCEESDAGKEELMKMRLPTRSDMICG
RLFDNANCPSLQNKPKMFFIQACRGDETDRGVDQQDGKNHTQSPGCEESDAGKEELMKMRLPTRSDMICG
RLFDNANCPSLQNKPKMFFIQACRGDETDRGVDQQDGKNHTQSPGCEESDAGKEELMKMRLPTRSDMICG
              ↖290       ↖300       ↖310       ↖320       ↖330       ↖340       ↖350

       ↙370       ↙380       ↙390       ↙400       ↙410       ↙420       ↙430
YACLKGNAAMRNTKRGSWYIEALTQVFSERACDMHVADMLVKVNALIKEREGYAPGTEFHRCKEMSEYCS
YACLKGNAAMRNTKRGSWYIEALTQVFSERACDMHVADMLVKVNALIKEREGYAPGTEFHRCKEMSEYCS
YACLKGNAAMRNTKRGSWYIEALTQVFSERACDMHVADMLVKVNALIKEREGYAPGTEFHRCKEMSEYCS
              ↖360       ↖370       ↖380       ↖390       ↖400       ↖410       ↖420

       ↙440       ↙450
TLCQQLYLFPGYPPT
TLCQQLYLFPGYPPT
TLCQQLYLFPGYPPT
              ↖430
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